nuclear-encoded proteins, as shown for *P. chromatophora*, we must abandon the paradigm that organelle births are exceptionally rare in eukaryote evolution.

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Brain Oscillations: Phase-Locked EEG Alpha Controls Perception

New research suggests that auditory stimuli can reset human oscillatory activity in visual cortex. This change in rhythmical brain activity leads to modulation of visual perception.

Paul Sauseng

When visual stimuli are presented very briefly, we tend to consciously perceive some of them and miss others. Whether we perceive such stimuli or not seems to be a matter of chance, but could there be fluctuations in perceptual threshold based on spontaneous brain activation patterns in the visual cortex? If this is the case, how are these patterns influenced or modulated by neural or environmental events? In this issue of Current Biology, Romei *et al.* [1] report that the instantaneous phase of rhythmical brain activity around 10 Hz — known as alpha activity, 100 ms wavelength — in the human primary visual cortex is reset by brief auditory stimuli. This was probed by delivering transcranial magnetic stimulation (TMS) to the primary visual cortex with different latencies after auditory stimulation. When the visual cortex is stimulated with TMS, single pulses, at a high enough intensity, elicit action potentials in V1 leading to the perception of a light flash, known as a phosphene. An increased likelihood of perceiving a phosphene was reported when a TMS pulse had been delivered around 100 or 200 ms after onset of a brief auditory stimulus. Phosphene perception was thus modulated at a timescale equal to two periods of phase-locked alpha waves (see Figure 1 for schematic results).

In a second experiment, Romei *et al.* [1] combined electroencephalographic (EEG) recordings with TMS to investigate more directly the association between auditory-evoked alpha oscillations (alpha waves time- and phase-locked to the brief auditory stimuli) and phosphene perception. Auditory stimuli not only led to significant phase-locking of alpha waves at recording sites over the auditory cortex, but significant phase-locking was also observed over visual cortex. The instantaneous phase of parieto-occipital alpha oscillations was significantly correlated to phosphene perception for at least two complete alpha periods (200 ms). Furthermore, reactivity of visual alpha amplitude to magnetic stimulation of occipital cortex (amplitude decrease as a marker of cortical excitability) was modulated in the same cyclic way as alpha waves evoked by auditory stimuli (see Figure 1 for an illustration of main findings). Cross-modal phase-resetting of alpha oscillations has been reported previously in monkeys [2], but Romei *et al.* [1] demonstrate similar effects of evoked alpha waves on visual perceptual processing in humans.

These exciting results suggest that stimulation of one sensory modality can lead to a strictly timed activation pattern in primary sensory cortex of another modality. The strict timing is possibly indicative of the temporal structure of cross-modal processing in the brain. Moreover, the new findings of Romei *et al.* [1] have important implications for the functional interpretation of oscillatory alpha activity. They provide evidence that evoked alpha waves at brain areas not associated with the primary sensory processing of a stimulus, for example, the visual cortex in auditory stimulation, are functionally relevant and not just an epiphenomenon. Klimesch and colleagues [3] suggested that the instantaneous phase of alpha activity at task-relevant brain areas is important for the specific timing of neural processes. This has been convincingly shown by Haegens *et al.* [4], who demonstrated that single cell firing patterns were modulated by alpha oscillations. However, increased alpha activity in brain areas not directly involved in information processing is considered to reflect inhibition of task-irrelevant brain areas [3]. Indeed, there is a classical view stating that alpha activity is associated with center-surround inhibition. For example, if a movement is performed, decreased excitatory alpha amplitude can be observed over sensorimotor areas with increased inhibitory alpha amplitude observed over occipital sites. In the case of processing of visual material, one might find exactly the opposite pattern [5]. The results of Romei *et al.* [1], however, suggest that alpha phase-dependent neural timing processes can also be observed over seemingly task-irrelevant brain areas and not only over task-relevant cortical regions.

So where does this leave our understanding of the functional meaning of alpha oscillations in humans? Is alpha activity not reflecting inhibition of cortical processing at all? Does alpha phase control neural processing on a millisecond scale independently of whether a brain area is relevant or irrelevant to the task?

Visually evoked potentials recorded from posterior sites in the human EEG typically show a positive deflection around 100 ms after onset of a visual stimulus. This so-called 'P1 component' has recently been associated with evoked alpha activity and inhibitory mechanisms [6]. The results presented by Romei *et al.* [1], however, suggest that visual perceptional threshold is decreased around 100 ms after stimulus onset, arguing for increased cortical excitability in the time window in which the P1 component can be found. Does this mean that the P1 component of visual evoked potentials does not reflect inhibitory processes? When addressing this question, we have to bear in mind that Romei *et al.* [1] used auditory stimuli to evoke alpha oscillations in visual cortex. Therefore, these fluctuations of excitability in visual areas are not directly comparable with brain potentials evoked by visual stimuli, and the effective time window in Romei *et al.*'s [1] study does not directly map onto the P1 time window of visually evoked potentials.

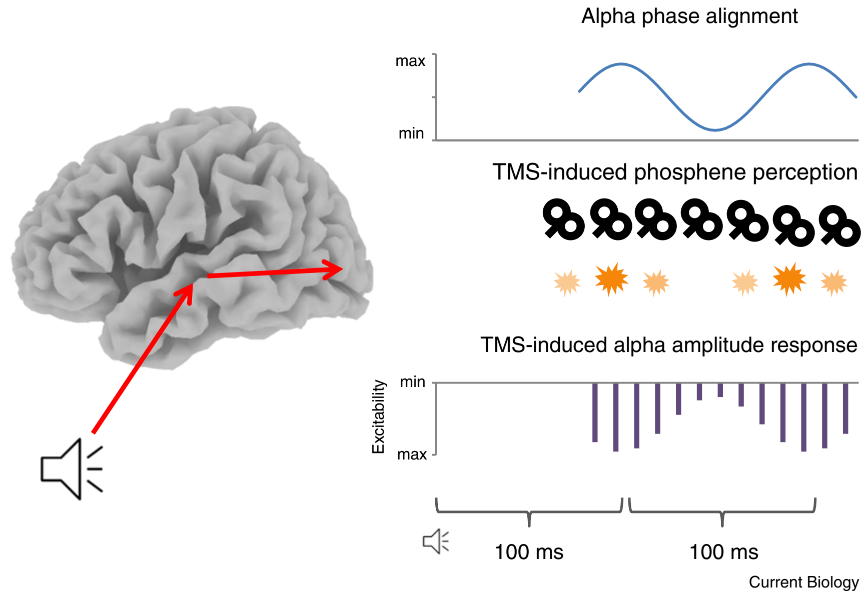

Figure 1. Schematic illustration of main findings reported by Romei *et al.* [1].
Presentation of an auditory stimulus elicits evoked, phase-locked alpha activity in visual cortex. Phase-locked alpha activity modulates reactivity (excitability) of the visual cortex and TMS-induced phosphene perception.

Instead of evoked alpha waves in visual areas being associated with primary processing of a visual stimulus, in the work of Romei *et al.* [1] it seems as if evoked alpha would reflect anticipatory processing, phase- and time-locked to presentation of an auditory stimulus. In most trials, the auditory stimulus was followed by a TMS pulse over the visual cortex, partly eliciting perception of a phosphene. The subject's task was to report perception of these phosphenes. Therefore, the auditory stimulus most likely acted as a kind of warning signal, priming activity in visual cortex for the perceptual task. In this context, it is notable that the effects reported by Romei *et al.* [1] were prominently found in a slower alpha frequency band, a frequency range classically associated with anticipation of task-relevant stimuli [7,8]. Anticipatory processes usually result in a reduction of (slow) alpha amplitude instead of increased alpha activity, but this is observed for non-phase-locked alpha activity. However, Romei *et al.* [1] report effects of evoked alpha waves. Freunberger and collaborators [9] demonstrated that evoked and induced (non-phase-locked) oscillatory activity in the alpha frequency range can reflect differential mechanisms. Taking this previous research on the functional meaning of alpha activity into account, the new findings of Romei *et al.* [1] suggest that rhythmical cortical activity around 10 Hz over seemingly task-irrelevant brain areas can fulfill inhibitory as well as neural timing functions similar to those previously discussed for task-relevant brain areas [3]: Spontaneous, non-phase-locked alpha activity reduces cortical excitability [10–12] on a rather large temporal scale, whereas evoked (phase-locked) alpha activity controls neural activation with high temporal precision [3,4,6], leading to control of visual perception.

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